STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number:

TO: Karen A Lacourciere Location: CM1/11D03/11E12 Art Unit : 1635 Friday, November 14, 2003 Case Serial Number: 09/813930	From : Susan Hanley Location: Biotech-Chem Library CM1 6B05 Phone: 305-4053 susan.hanley@uspto.gov

Search Notes

```
=> d que
L18       18520 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRIIODOTHYRONINE/CT
L19       24629 SEA FILE=MEDLINE ABB=ON  PLU=ON  THYROXINE/CT
L43       51709 SEA FILE=MEDLINE ABB=ON  PLU=ON  1000
L44        1413 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43(2A)(CONCENTRATION OR
                NG(W)DL)
L46           4 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L18 OR L19) AND L44
```

only #3 shown

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=> d ibib abs trial 3

L46  ANSWER 3 OF 4     MEDLINE on STN
ACCESSION NUMBER:   85078037     MEDLINE
DOCUMENT NUMBER:    85078037   PubMed ID: 6595195
TITLE:              T3-hyperthyroidism caused by enhanced and shifted
                    T4-conversion.
AUTHOR:             Loos U; Keck F S; Grau R
SOURCE:             HORMONE AND METABOLIC RESEARCH. SUPPLEMENT, (1984) 14
                    85-93.
                    Journal code: 0330417. ISSN: 0170-5903.
PUB. COUNTRY:       GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        198502
ENTRY DATE:         Entered STN: 19900320
                    Last Updated on STN: 19970203
                    Entered Medline: 19850205
AB   Radioactivities of endogenously labelled thyroid hormones following in
     vivo application of 131 I and extraction from serial blood samples, show
     that T4 secretion is enhanced in T3-hyperthyroidism as it is in
     T4-T3-hyperthyroidism.  In an extreme case of T3-hyperthyroidism with
     serum concentrations (SC) of T3 nearly equal to T4 (1000
     ng/dl and 1800 ng/dl, respectively) tracer studies
     revealed a very short half life of T4 when compared to T3 (21.8 and 20.2
     hrs., respectively).  In 110 cases with both types of hyperthyroidism,
     regression analysis showed that T3/T4 ratio as an indicator of T4
     conversion, as well as T3/rT3 ratio as an indicator of the direction of
     the conversion, are related to T4SC (r = -0.84 and -0.72, respectively, p
     less than 0.001).  T3-hyperthyroidism is described by high values of these
     ratios.  For the definition of T3-hyperthyroidism it is suggested that
     both T4 and rT3SC are within the normal range (T4 less than or equal to
     11.5 micrograms/dl, rT3 less than or equal to 43.0 ng/dl) and according to
     this definition, T3/rT3 is higher than in T4-T3-hyperthyroidism and in an
     undefined group (24.8 +/- 4.5 vs. 6.3 +/- 0.4 or 7.5 +/- 0.4,
     respectively).  By means of the ratios the undefined group may be
     allocated to T4-T3-hyperthyroidism.  The T3/rT3 ratio is value of greater
     than 10 has a frequency of 88% in thus defined T3-hyperthyroidism and a
     ratio of less than or equal to 10 is found in 90% of the other
     cases.(ABSTRACT TRUNCATED AT 250 WORDS)
TI   T3-hyperthyroidism caused by enhanced and shifted T4-conversion.
CT   Check Tags: Human; Support, Non-U.S. Gov't
      Granulocytes: ME, metabolism
      Hyperthyroidism: BL, blood
     *Hyperthyroidism: ET, etiology
      Iodine Radioisotopes: DU, diagnostic use
      Kinetics
      Subcellular Fractions: ME, metabolism
        Thyroxine: BL, blood
       *Thyroxine: ME, metabolism
        Triiodothyronine: BL, blood
       *Triiodothyronine: PH, physiology
      Triiodothyronine, Reverse: BL, blood
RN   5817-39-0 (Triiodothyronine, Reverse); 6893-02-3 (Triiodothyronine);
     7488-70-2 (Thyroxine)
CN   0 (Iodine Radioisotopes)
```

```
=> d que l69
L68           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  1000(2A)NG(W)DL
L69           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 AND T4/TI


=> d ibib abs hitstr ind l69

L69  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        1982:116066  HCAPLUS
DOCUMENT NUMBER:         96:116066
TITLE:                   Characterization of an automated radioimmunoassay for
                         T4, T3, T3U, and FTI
AUTHOR(S):               Valdes, Roland, Jr.; Useted, John T.
CORPORATE SOURCE:        Jew. Hosp. St. Louis, St. Louis, MO, 63110, USA
SOURCE:                  Annals of Clinical and Laboratory Science (1982),
                         12(1), 42-50
                         CODEN: ACLSCP; ISSN: 0091-7370
DOCUMENT TYPE:           Journal
LANGUAGE:                English
GI
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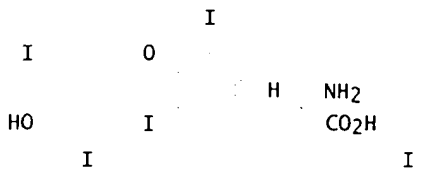


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AB   The performance characteristics are reported for assays of thyroxine (I)
     [51-48-9], triiodothyronine (T3) [6893-02-3], and T3-uptake (T3U) by
     using the Gammaflo automated assay system. A comparison of calcd. free I
     index (FTI) values also is presented. This automated RIA system utilizes
     a combination of continuous-flow methodol. and chromatog. sepn.
     techniques. The I assay had a std. curve range of 1.5-24.0 .mu.g/dL. The
     intra- and interassay relative std. deviations were 4.3 and 5.3%, resp.,
     for a I concn. of 10.0 .mu.g/dL. The T3 assay had a std. curve range of
     50-1000 ng/dL, and the corresponding
     relative std. deviations were 7.3 and 7.1%, resp., for a concn. of 213
     ng/dL. The automated serum I and T3 results correlated (r = 0.966 and
     0.864) with a manual radioimmunoassay procedure. Intra-assay and
     interassay relative std. deviations for a mid-range normal 30.1% T3U value
     were 6.2 and 4.9%, resp. Ref. range comparison of FTI by both automated
     and manual results correlated for 47 out of 51 patients compared. This
     automated system appears to offer a viable alternative to I, T3, and T3U
     manual RIA techniques in terms of operational simplicity, anal.
     performance, and sample through-put flexibility.
CC   2-1 (Mammalian Hormones)
ST   automated radioimmunoassay T4 T3
IT   Blood analysis
        (thyroxine and triiodothyronine detn. in, of human by automated
        radioimmunoassay)
IT   6893-02-3
     RL: ANT (Analyte); ANST (Analytical study)
        (detn. of, in human blood serum by automated radioimmunoassay)
IT   51-48-9, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (detn. of, in human blood serum by automated radioimmunoassay, free
        thyroxine index detn. in relation to)
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=> d que l84
L77        1544 SEA FILE=EMBASE ABB=ON  PLU=ON  NG(W)DL
L78         499 SEA FILE=EMBASE ABB=ON  PLU=ON  L77 AND (T3 OR T4 OR THYROXINE
                OR TRIIODOTHYRONINE)
L80         152 SEA FILE=EMBASE ABB=ON  PLU=ON  L78 AND ELEVAT?
L81         110 SEA FILE=EMBASE ABB=ON  PLU=ON  L80 AND HUMAN
L82          42 SEA FILE=EMBASE ABB=ON  PLU=ON  L81 AND HYPERTHY?
L83          41 SEA FILE=EMBASE ABB=ON  PLU=ON  L82 AND PY<2001
L84           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L83 AND (SHORT OR CONSEQUENCES
                OR ORAGRAFIN)/TI


=> d ibib abs ind 1-3

L84  ANSWER 1 OF 3  EMBASE  COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ACCESSION NUMBER:   88120995  EMBASE
DOCUMENT NUMBER:    1988120995
TITLE:              Short stature and thyroxine-binding
                    globulin excess: Improvement with triiodothyronine
                    treatment.
AUTHOR:             Alain N.; Zipf W.B.
CORPORATE SOURCE:   Department of Pediatrics, Children's Hospital, Ohio State
                    University, Columbus, OH 43205, United States
SOURCE:             Pediatrics, (1988) 81/5 (674-679).
                    ISSN: 0031-4005  CODEN: PEDIAU
COUNTRY:            United States
DOCUMENT TYPE:      Journal
FILE SEGMENT:       003     Endocrinology
                    007     Pediatrics and Pediatric Surgery
                    022     Human Genetics
                    037     Drug Literature Index
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Thyroxine-binding globulin (TBG) excess with increased total
     thyroxine (T4) and triiodothyronine (
     T3) levels has not been thought to produce symptoms. We report on
     a white boy, initially seen at 4.3 years of age and observed for 4 years,
     who has short stature caused by the excess thyroxine binding. At
     his initial examination his thyroxine-binding globulin (TBG)
     levels were elevated (17 mg/dL), and he had a T4 level
     of 25.8 .mu.g/dL, short stature, a bone age of 19 months, normal vital
     signs, and hyperthyroid-stimulating hormone (TSH) response to
     thyrotropin-releasing hormone (TRH) testing (maximal value 58 .mu.IU/mL).
     Results of tests obtained during the next 6 months showed other
     abnormalities related to thyroid function. Tests showed the following
     values: T3 412 ng/dL, thyroid uptake 24%,
     and low T3 resin uptake. They also showed these values: an
     elevated basal TSH of 8.7 .mu.IU/mL, a slightly low preejection
     period to left ventricular ejection time ratio of 0.29 (normal 0.35 .+-.
     0.04), and WISC-R IQ within normal limits. Because of the persistent short
     stature, T3 supplementation was started at age 7 years and
     gradually increased to 35 .mu.g/d. The patient showed no thyrotoxic
     symptoms. Serum T4 level decreased from 25.8 to 4.2 .mu.g/dL,
     T3 increased to 1,240 ng/dL, the TRH/TSH test
     result was suppressed (maximal level 1.8), and the preejection period to
     left ventricular ejection time ratio decreased to 0.24. Growth velocity
     increased by 65%. Both of the child's parents had normal thyroid test
     results. A younger brother also showed similar elevations of TBG
     level and even greater T4 values (36 .mu.g/dL). His height had
     remained at the 25th percentile. This observation is the first report of
     the recessive transmission of TBG excess and suggests an associated
     thyroid-dependent short stature that is correctable with treatment.
CT   Medical Descriptors:
     *hypothyroidism: DI, diagnosis
     *hypothyroidism: DT, drug therapy
     bone age
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growth
heredity
hyperthyroxinemia
preschool child
short stature
priority journal
case report
human
male
oral drug administration
Drug Descriptors:
liothyronine
RN (liothyronine) 6138-47-2, 6893-02-3

L84 ANSWER 2 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 83205194 EMBASE
DOCUMENT NUMBER: 1983205194
TITLE: The **consequences** of inappropriate treatment because of failure to recognize the syndrome of pituitary and peripheral tissue resistance to thyroid hormone.
AUTHOR: Refetoff S.; Salazar A.; Smith T.J.; Scherberg N.H.
CORPORATE SOURCE: Thyroid Study Unit, Dep. Med., Univ. Chicago Sch. Med., Chicago, IL 60637, United States
SOURCE: Metabolism: Clinical and Experimental, (1983) 32/8 (822-834).
CODEN: METAAJ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
029 Clinical Biochemistry
007 Pediatrics and Pediatric Surgery
006 Internal Medicine
049 Forensic Science Abstracts
LANGUAGE: English
AB Since the description of the syndrome of global (peripheral tissues and pituitary) resistance to thyroid hormone, new cases are being recognized with increasing frequency. The patient described herein had a markedly **elevated** serum TSH concentration of 260 .mu.U/mL at the time of diagnosis. Studies suggest that **elevations** of serum TSH levels in this and other patients with the syndrome are most likely iatrogenic in origin. The patient was 31/2 years old when a goiter and a high serum **T4** concentration were detected. Despite subtotal thyroidectomy, antithyroid drugs were required to maintain her **T4** level in the normal range. She was referred at age 111/2 years because of recurrent goiter. Her parents and five older siblings had normal thyroid function. Off therapy, her serum **T4** level was 14.9 .mu.g/dL, FT4I was 17.0, **T3** was 362 **ng/dL**, TSH was 260 .mu.U/mL, and antibodies were negative. There were no signs of thyrotoxicosis, her bone age was 7 years, her growth was stunted (third percentile), her intellectual quotient (IQ) was 67, and there was a 30-50 dB sensorineural hearing loss. The presence of a pituitary adenoma was ruled out. Her TSH had normal bioreactivity and rose to 540 .mu.U/mL in response to TRH. **Triiodothyronine** was given in incremental doses of 50, 100, 200, and 400 .mu.g/d over 28 days. The log concentrations of serum TSH showed an inverse linear correlation with serum **T3**. While receiving the highest dose of **T3**, on which the level of serum **T3** ranged from 1,400 to 2,500 **ng/dL**, the TSH response to TRH normalized (basal 4.2 and peak 20 .mu.U/mL), as did the high levels of serum cholesterol, carotene, and **T4**. Her BMR rose from +5 to +22%, her IQ rose to 77, and she gained weight without an increase in caloric intake. Only minimal changes were observed in levels of urinary cAMP, hydroxyproline, magnesium, and nitrogen. All values, with the exception of the weight gain, returned to baseline 2 months after **T3** treatment was discontinued. The TSH level was suppressed by L-dopa and by prednisone. Long-term therapy with equivalent

doses of **T4** (from 300 to 1,000 .mu./d) produced a growth of 3 cm during the initial 6 weeks, 10.5 cm over the ensuring year (above the 10th percentile), and regression of goiter without thyrotoxicosis. The patient exhibited resistance to thyroid hormone in pituitary and peripheral tissues. The optimal dose of **T4** replacement could be predicted by studying tissue responses to incremental doses of **T3**. The marked **elevation** in serum TSH concentration, stunted growth, and laboratory evidence of hypothyroidism were due to the limited thyroidal reserve caused by thyroidectomy. All patients with an impaired ability to compensate for the defect as a result of inappropriate treatment should be given thyroid hormone in amounts short of producing catabolic effects. Such a dose is expected to normalize the basal serum TSH concentration and its response to TRH.

CT Medical Descriptors:
*drug resistance
*goiter
*hyperthyroidism
*hypophysis
*drug therapy
cholesterol blood level
thyroidectomy
endocrine system
therapy
human
diagnosis
clinical article
Drug Descriptors:
*levodopa
*liothyronine
*prednisone
*protirelin
*thiamazole
*thyroid hormone
*thyrotropin
*thyroxine
carotene

RN (levodopa) 59-92-7; (liothyronine) 6138-47-2, 6893-02-3; (prednisone) 53-03-2; (protirelin) 24305-27-9; (thiamazole) 60-56-0; (thyrotropin) 9002-71-5; (**thyroxine**) 7488-70-2

L84 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 83007668 EMBASE
DOCUMENT NUMBER: 1983007668
TITLE: Comparison of sodium ipodate (**Oragrafin**) and propylthiouracil in early treatment of **hyperthyroidism**.
AUTHOR: Wu S.Y.; Shyh T.P.; Chopra I.J.; et al.
CORPORATE SOURCE: Dep. Med., VA Med. Cent., Long Beach, CA 90822, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1982) 54/3 (630-634).
CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
030 Pharmacology
LANGUAGE: English

AB To investigate further the usefulness of sodium ipodate (Oragrafin) in the management of **hyperthyroidism**, we studied the effects of a 21-day treatment of Graves' disease patients with either ipodate (1 g/day) or propylthiouracil (PTU; 600 mg/day) on serum **T3**, **T4**, rT3, pulse rate, pulse pressure, and body weight. Baseline serum concentrations of immunoassayable **T3**, **T4**, and rT3 were (mean .+-. SEM) 405 .+-. 64 **ng/dl**, 20.9 .+-. 3.9 .mu.g/dl, and 142 .+-. 20 **ng/dl**, respectively, in the

ipodate-treated group (n = 16) and 504 .+-. 87 **ng/dl**,
23.0 .+-. 3.6 .mu.g/dl, and 164 .+-. 29 **ng/dl**,
respectively, in the PTU-treated group (n = 6). Within 24 h after the
first doses of ipodate, serum **T3** decreased by 58% (P < 0.005),
remained decreased thereafter (67-76%), and stayed within the normal range
throughout treatment. The decreases in serum **T3** concentration in
the PTU-treated group of 23% of 24 h, 27% at 72 h, and 56% on day 21 were
significantly less than the corresponding values in the ipodate group. At
24 h the serum **T4** concentration decreased by 20% (P < 0.05) in
the ipodate group, while it did not change in the PTU group. Subsequently,
the serum **T4** concentration was 36-47% lower than baseline in the
ipodate group. It decreased more slowly in PTU-treated patients to 25%
below baseline on day 7 (P = NS), 35% on day 14 (P < 0.05), and 45% on day
17 (P < 0.05). The serum concentration of rT3 was markedly
elevated (73-276% above baseline; P < 0.05) after treatment with
ipodate, whereas it decreased significantly (35% below baseline; P < 0.05)
on day 10 and thereafter in patients receiving PTU. When the percent
changes in circulating thyroid hormone levels in the two groups were
compared using the areas under the serum concentration curves, the fall in
serum **T3** and the rise in serum rT3 were significantly greater in
the ipodate group than in the PTU group, but the decreases in the serum
T4 levels were similar. Resting pulse rate and pulse pressure
decreased and body weight increased in both groups, but statistically
significant changes were observed earlier with ipodate than with PTU. The
data suggest that (1) ipodate (1 g/day, orally) compares favorably with
PTU (600 mg/day, orally) in reducing circulating **T3** and
T4 and clinical **hyperthyroidism** in patients with Graves'
disease; and (2) ipodate may serve as a useful adjunct in the early
treatment of **hyperthyroidism.**

CT Medical Descriptors:
*drug comparison
  ***hyperthyroidism**
*drug therapy
clinical article
therapy
  human
endocrine system
Drug Descriptors:
*iopodate sodium
*liothyronine
*propylthiouracil
  ***thyroxine**

RN (iopodate sodium) 1221-56-3; (liothyronine) 6138-47-2, 6893-02-3;
(propylthiouracil) 51-52-5; (**thyroxine**) 7488-70-2

CN Oragrafin

10831 2

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: Karen Lacoureiere

Serial Number: 09/913,930

Date: 11-13-03 Phone: 703 308 7523 Art Unit: 1635

mailbox 11E12, office 11D09

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please provide a reference teaching how high Thyroid levels get in humans: especially T_3 & T_4 levels hopelly T_4 levels above 1000 ng/dL ??

STAFF USE ONLY

Date completed: 11/14

Searcher: Hanley

Terminal time: 8

Elapsed time: PRP 45

CPU time:

Total time:

Number of Searches:

Number of Databases:

Search Site

- ____ STIC
- ____ CM-1
- ____ Pre-S

Type of Search

- ____ N.A. Sequence
- ____ A.A. Sequence
- ____ Structure
- X Bibliographic

Vendors

- ____ IG
- $331 STN
- ____ Dialog
- ____ APS
- ____ Geninfo
- ____ SDC
- ____ DARC/Questel
- ____ Other